

# PATENT COOPERATION TREATY

PCT DATE:	—
FORMALITIES:	JW / 1 R P C
PAT. OFF:	BF
ON PCT:	—
CASE NO:	PU0367-PCT

From the  
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

<p>To:</p> <p><b>FRANKS, Barry</b> Amersham plc Amersham Place Little Chalfont Buckinghamshire HP7 9NA GRANDE BRETAGNE</p>	<div style="border: 1px solid black; padding: 5px; width: fit-content; margin: 0 auto;"> <p><b>RECEIVED</b></p> <p>04 JAN 2006</p> </div>
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NOTIFICATION OF TRANSMITTAL OF  
THE INTERNATIONAL PRELIMINARY  
REPORT ON PATENTABILITY  
(PCT Rule 71.1)

Applicant's or agent's file reference <b>PU0367-PCT</b>			<b>IMPORTANT NOTIFICATION</b>
International application No. <b>PCT/EP2004/010599</b>	International filing date (day/month/year) <b>22.09.2004</b>	Priority date (day/month/year) <b>23.09.2003</b>	
Applicant <b>AMERSHAM BIOSCIENCES AB</b>			

1. The applicant is hereby notified that this International Preliminary Examining Authority transmits herewith the international preliminary report on patentability and its annexes, if any, established on the international application.
2. A copy of the report and its annexes, if any, is being transmitted to the International Bureau for communication to all the elected Offices.
3. Where required by any of the elected Offices, the International Bureau will prepare an English translation of the report (but not of any annexes) and will transmit such translation to those Offices.
4. **REMINDER**

The applicant must enter the national phase before each elected Office by performing certain acts (filing translations and paying national fees) within 30 months from the priority date (or later in some Offices) (Article 39(1)) (see also the reminder sent by the International Bureau with Form PCT/IB/301).

Where a translation of the international application must be furnished to an elected Office, that translation must contain a translation of any annexes to the international preliminary report on patentability. It is the applicant's responsibility to prepare and furnish such translation directly to each elected Office concerned.

For further details on the applicable time limits and requirements of the elected Offices, see Volume II of the PCT Applicant's Guide.

The applicant's attention is drawn to Article 33(5), which provides that the criteria of novelty, inventive step and industrial applicability described in Article 33(2) to (4) merely serve the purposes of international preliminary examination and that "any Contracting State may apply additional or different criteria for the purposes of deciding whether, in that State, the claimed inventions is patentable or not" (see also Article 27(5)). Such additional criteria may relate, for example, to exemptions from patentability, requirements for enabling disclosure, clarity and support for the claims.

Name and mailing address of the international preliminary examining authority:  <div style="display: flex; align-items: center;"> <div> <p>European Patent Office - P.B. 5818 Patentlaan 2 NL-2280 HV Rijswijk - Pays Bas Tel. +31 70 340 - 2040 Tx: 31 651 epo nl Fax: +31 70 340 - 3016</p> </div> </div>	Authorized Officer  <p><b>Smits, A</b> Tel. +31 70 340-3598</p> <div style="text-align: right;"> </div>
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# PATENT COOPERATION TREATY

## PCT

### INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference PU0367-PCT		<b>FOR FURTHER ACTION</b>		See Form PCT/PEA416
International application No. PCT/EP2004/010599		International filing date (day/month/year) 22.09.2004	Priority date (day/month/year) 23.09.2003	
International Patent Classification (IPC) or national classification and IPC B01D15/08, G01N30/60				
Applicant AMERSHAM BIOSCIENCES AB				
<p>1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.</p> <p>2. This REPORT consists of a total of 8 sheets, including this cover sheet.</p> <p>3. This report is also accompanied by ANNEXES, comprising:</p> <p>a. <input type="checkbox"/> sent to the applicant and to the International Bureau) a total of sheets, as follows:</p> <p><input type="checkbox"/> sheets of the description, claims and/or drawings which have been amended and are the basis of this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).</p> <p><input type="checkbox"/> sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.</p> <p>b. <input type="checkbox"/> (sent to the International Bureau only) a total of (indicate type and number of electronic carrier(s)) , containing a sequence listing and/or tables related thereto, in computer readable form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).</p>				
<p>4. This report contains indications relating to the following items:</p> <p><input checked="" type="checkbox"/> Box No. I Basis of the opinion</p> <p><input type="checkbox"/> Box No. II Priority</p> <p><input type="checkbox"/> Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability</p> <p><input type="checkbox"/> Box No. IV Lack of unity of invention</p> <p><input checked="" type="checkbox"/> Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement</p> <p><input type="checkbox"/> Box No. VI Certain documents cited</p> <p><input checked="" type="checkbox"/> Box No. VII Certain defects in the international application</p> <p><input checked="" type="checkbox"/> Box No. VIII Certain observations on the international application</p>				
Date of submission of the demand  20.04.2005		Date of completion of this report  03.01.2006		
Name and mailing address of the international preliminary examining authority:  European Patent Office - P.B. 5818 Patentlaan 2 NL-2280 HV Rijswijk - Pays Bas Tel. +31 70 340 - 2040 Tx: 31 651 epo nl Fax: +31 70 340 - 3018		Authorized Officer  Hilgenga, K  Telephone No. +31 70 340-2072 		

**INTERNATIONAL PRELIMINARY REPORT  
ON PATENTABILITY**

International application No.  
PCT/EP2004/010599

**Box No. I Basis of the report**

1. With regard to the **language**, this report is based on the international application in the language in which it was filed, unless otherwise indicated under this item.
- ☐ This report is based on translations from the original language into the following language , which is the language of a translation furnished for the purposes of:
- ☐ international search (under Rules 12.3 and 23.1(b))
  - ☐ publication of the international application (under Rule 12.4)
  - ☐ international preliminary examination (under Rules 55.2 and/or 55.3)
2. With regard to the **elements**\* of the international application, this report is based on *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report)*:

**Description, Pages**

1, 2, 4, 5, 7, 8                      as originally filed  
3, 6                                      as amended (together with any statement) under Art. 19 PCT

**Claims, Numbers**

2-6                                      as originally filed  
1    as amended (together with any statement) under Art. 19 PCT

**Drawings, Sheets**

1/7-7/7                                  as originally filed

- ☐ a sequence listing and/or any related table(s) - see Supplemental Box Relating to Sequence Listing

3. ☐ The amendments have resulted in the cancellation of:

- ☐ the description, pages
- ☐ the claims, Nos.
- ☐ the drawings, sheets/figs
- ☐ the sequence listing *(specify)*:
- ☐ any table(s) related to sequence listing *(specify)*:

4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).

- ☐ the description, pages
- ☐ the claims, Nos.
- ☐ the drawings, sheets/figs
- ☐ the sequence listing *(specify)*:
- ☐ any table(s) related to sequence listing *(specify)*:

\* If item 4 applies, some or all of these sheets may be marked "superseded."

**INTERNATIONAL PRELIMINARY REPORT  
ON PATENTABILITY**

International application No.  
PCT/EP2004/010599

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**Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

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**1. Statement**

Novelty (N)	Yes: Claims	4
	No: Claims	1,2,3,5,6
Inventive step (IS)	Yes: Claims	
	No: Claims	1-6
Industrial applicability (IA)	Yes: Claims	1-6
	No: Claims	

**2. Citations and explanations (Rule 70.7):**

**see separate sheet**

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**Box No. VII Certain defects in the international application**

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The following defects in the form or contents of the international application have been noted:

**see separate sheet**

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**Box No. VIII Certain observations on the international application**

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The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

**see separate sheet**

**Re Item V**

**Reasoned statement with regard to novelty, inventive step or industrial applicability;  
citations and explanations supporting such statement**

1. The following document is referred to in this communication:

D1 : US 6 224 760 B1 (DAVIES JOHN ET AL) 1 May 2001 (2001-05-01)

2. The under **Re Item VIII** mentioned lack of clarity notwithstanding, the subject-matter of claim 1 is not new in the sense of Article 33(2) PCT, and therefore the criteria of Article 33(1) PCT are not met.

Document D1 (see figure 3; column 2, lines 13-24 ; column 3 , lines 32-65 ) discloses a chromatography column distribution system comprising a set of first bed support ribs extending radially from an inner, first radial position R1 near the centre of a plate to an outer radial position nearer to the periphery of the plate and at least one set of intermediate bed support ribs starting at an intermediate radial position and extending to an outer radial position nearer to the periphery of the plate, whereby channels are formed between adjacent bed support ribs.

For this document, the desired local effective channel height is construed as the actual effective channel height which necessarily varies in accordance with a formula from the first radial position R1 to the outer radial position.

Thus, the transverse cross-sectional areas of the ribs or channels in D1 are constructed such that the actual local effective channel height is in fact the desired local effective channel height over the area covered by the distribution system.

Therefore, the actual local effective channel height is within 15% of the desired local effective channel height over portions of the distribution system situated between the first radial position R1 and the outer radial position, wherein the total length of said portions correspond to at least 80% of the distance between said first radial position R1 and said outer radial position.

As can be seen from the above, D1 discloses all the features defined in independent claim 1.

Furthermore, D1 discloses also the subject-matter of dependent claims 2, 3, 5, 6.

Hence, the subject-matter of claims 1, 2, 3, 5, 6 is not new in view of document D1 (Article 33(2) PCT).

**3** The subject-matter of independent claim 4 differs from the chromatography column distribution system of D1 in that:

The desired local effective channel height varies inversely in proportion to the radial distance from the center of the column and the transverse cross-sectional areas of said ribs or said channels are adapted such that the actual local effective channel height is within 15% of this desired local effective channel height over portions of the distribution system situated between the first radial position R1 and the outer radial position, wherein the total length of said portions correspond to at least 80% of the distance between said first radial position R1 and said outer radial position.

The subject-matter of dependent claim 4 is therefore novel (Article 33(2) PCT).

However, the subject-matter of claim 4 does not involve an inventive step in the sense of Article 33(3) PCT, and therefore the criteria of Article 33(1) PCT are not met for the following reasons:

The problem to be solved by the present invention may be regarded as to provide a column chromatography distribution system comprising different set of support ribs extending radially, starting at different radial positions and radial distribution channels which shows a linear decrease of the local effective channel height with the radial distance from the center of the column without any or with reduced discontinuity, preventing thereby local pressure increase and throttling of the fluid flow in the radial distribution channels over most of the area covered by the distribution system.

The solution to this problem proposed in claim 4 of the present application is not

considered as involving an inventive step (Article 33(3) PCT) for the following reasons:

When formulating the problem and due to a lack of alternatives creating thereby a 'one-way street' situation, the man skilled in the art would necessarily think of adapting the cross-sectional area of the channels available for the fluid at each radial position, for example adapting the width of the channels by changing the width of the ribs at any radial position, in order to obtain a linear decrease of the local effective channel height with the radial distance from the center of the column and without any or with reduced discontinuity of the cross sectional area of the channels thereby preventing local pressure increase and throttling of the fluid flow.

The man skilled in the art would also try to optimise this system such that the discontinuities of the cross-sectional area of the channels which causes the local pressure increase and throttling of the fluid flow is as low as possible on most of the area covered, thereby arriving at something falling within the terms of claim 4.

**Re Item VII**

**Certain defects in the international application**

1. Claim 4 should read "in that said **desired local effective channel height** varies inversely in proportion to the radial distance from **the center of the column**" (see description, page 8, line 14).

2. Page 7, lines 18-19 of the description which describes the graph of figure 4 is inconsistent with what is actually shown by this graph:

The graph actually shows an actual effective channel height of 1.4 mm at  $R=110$  mm and not 1.6 mm as indicated in the description.

3. Page 8, lines 13 and 17 of the description should probably read "channel height" and not "column height".

4. Page 3, line 5 should probably read "R=110 mm" and not "R=112 mm".
5. Page 6, line 30, "the" in the wording ".....at any radial position is **the** adapted to partly or completely....." should be removed.

**Re Item VIII**

**Certain observations on the international application**

In claim 1, the wording "**....the desired local effective channel height is intended to vary in accordance with a predetermined formula** from said first radial position R1 to said outer radial position characterised in that the transverse cross-sectional areas of said ribs or said channels are **adapted such that the actual local effective channel height is within 15% of the desired local effective channel height** over portions of the distribution system....." does not clearly define the technical features of the chromatography column distribution system.

As a matter of fact, "**the desired local effective channel height which is intended to vary in accordance with a predetermined formula**" does not provide any technical feature concerning this particular desired local effective channel height since the predetermined formula is unspecified.

Furthermore, the claim attempts to define the **actual local effective channel height** with respect to this unclear and undetermined **desired local effective channel height**, rendering thereby the **actual local effective channel height** also unclear.

Thus, claim 1 does not meet the requirements of Article 6 PCT in that the matter for which protection is sought is not clearly defined.

The same applies to dependant claims 2, 3, 5, 6.



3 (amended)

shows the calculated effective channel height (ECH) against radial distance (R) from the centre of the column for a typical prior art column with ribs starting at R=55 mm and R=110 mm, while the dotted line shows the desired linear variation in local effective channel height. At R=55 mm the actual local effective channel height is 3.2 mm while the desired local effective channel height is 3.8 mm, i.e. only 84% of the desired value, and at R=112 mm the actual local effective channel height is 1.4 mm – only 56% of the desired height is 2.5 mm. Clearly, there is a local decrease in the effective channel height, and therefore throttling of the flow in the distribution channels, at the radial positions where the number of ribs doubles. This causes a local pressure increase which has a negative impact on the chromatographic performance.

#### Summary of the Invention

According to the present invention, at least some of the problems with the prior art are solved by means of a device having the features present in the characterising part of claim 1.

#### Brief Description of the Figures

Figure 1a) shows schematically a plan view of a prior art distribution plate for a chromatography column;

Figure 1b) shows a cross-section along line I-I in figure 1a);

Figure 1c) shows an enlarged view of a portion of the plan view of figure 1a);

Figure 1d) shows a perspective view of the portion of the prior art distribution plate shown in figure 1c);

Figure 2a) shows schematically a plan view of a first embodiment of a chromatography column distribution plate in accordance with the present invention.

Figure 2b) shows an enlarged view of a portion of the plan view of figure 2a);

first intermediate radial position R2 to the outer radial position near to the periphery 109 of the body 103.

Starting at a second inner intermediate radial position R3 situated between the orifice 105 and the periphery 109 at a distance greater than R2 from the orifice 103, a plurality of second intermediate, bed support ribs 119 of length LL3 are positioned between the first bed support ribs 7 and the first intermediate bed support ribs 117. Each second bed support rib 119 has a tapered portion 121 of length t13 which has a pointed end that faces towards the central inlet orifice 105, and an elongated rib body 123 of length (LL3-t13) with a varying width. These second intermediate bed support ribs 119 extend from second inner intermediate radial position R2 to the outer radial position near to the periphery 109 of the body 103.

Channels 113 are formed by the gaps between the ribs 107, 117, 119. In this embodiment the local effective channel height decreases in a more linear manner than in prior art devices (i.e. the maximum difference between the desired local effective channel height and the actual local effective channel height is less than 15.5% of the desired local channel height) from the position R1 to the periphery of the column). This is achieved by the widths of the elongated rib bodies 111, 118 and 123 being varied along their lengths in order to reduce or eliminate discontinuities (that is, abrupt local changes) in the cross sectional area of the channels 113 formed between ribs. This may be achieved by adapting the width of the elongated body 111 of each first support rib 107 at the position along its length where it is adjacent the tapered portion 116 of a first intermediate support rib 117 and/or second intermediate support rib 119 and/or by adapting the width of the elongated body 118 of each first intermediate support rib 117 at the position along its length where it is adjacent the tapered portion 121 of a second intermediate support rib 119 so that the actual local effective channel height is at worst within 15% of, preferably is within 10% of, more preferably is within 5% of, and most preferably is the same as the desired local effective channel height. In order to reduce discontinuities in the cross sectional area of a channel at the radial positions where there are first and second intermediate support ribs 117, 119, the width of each elongated body 111 at any radial position is adapted to partly or completely compensate for the reduction in channel cross sectional area caused by the presence of the intermediate support rib 117 so that the actual local effective channel height is at worst within 15% of the desired local channel height. Preferably the actual local effective channel height is within 10% of, more preferably it is

## Claims

1. Chromatography column distribution system (101) comprising a set of first bed support ribs (107) extending radially from a inner, first radial position (R1) near the centre of the plate to a outer radial position nearer to the periphery (109) of the plate and at least one set of intermediate bed support ribs (117, 119) starting at an intermediate radial position (R2, R3) and extending to an outer radial position nearer to the periphery (109) of the plate (101), whereby channels are formed between adjacent bed support ribs (107, 117, 119) and the desired local effective channel height is intended to vary in accordance with a predetermined formula from said first radial position R1 to said outer radial position, characterised in that the transverse cross-sectional areas of said ribs (107, 117, 119) or said channels are adapted such that the actual local effective channel height is within 15% of the desired local effective channel height over portions of the distribution system situated between said first radial position (R1) and said outer radial position, wherein the total length of said portions correspond to at least 80% of the distance between said first radial position (R1) and said outer radial position.
2. Chromatography column distribution system (101) in accordance with claim 1 characterised in that the transverse cross-sectional areas of said ribs (107, 117, 119) or said channels are adapted such that the actual local effective channel height is within 10% of the desired local effective channel height.
3. Chromatography column distribution system (101) in accordance with claim 1 or claim 2 characterised in that the transverse cross-sectional areas of said ribs (107, 117, 119) or said channels are adapted such that the actual local effective channel height is within 5% of the desired local effective channel height.
4. Chromatography column distribution system (101) in accordance with any of the previous claims characterised in that said local effective channel height varies inversely in proportion to the radial distance from (R1).
5. Chromatography column distribution system (101) in accordance with any of the previous claims characterised in that said portions correspond to at least 90% of the distance between said first radial position (R1) and said outer radial position.